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THE USE AND ABUSE OF BACTERIAL THERAPY *

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As one of the earlier pupils of Wright at St. Mary's Hospital, London, I trust that some of the things I shall say in the discussion of this subject may not seem to be at variance with the teachings of that brilliant student of immunity. There can be no doubt of the value of his researches and their practical application in that realm of medicine with which we are so frequently concerned. But as often happens with any more or less complicated and difficult mode of procedure, the method has been misunderstood and misapplied by many whose optimism carried them further than the facts warranted. It will not be necessary to discuss in detail the features of immunity conferred by the inoculation of bacterial cells or their products in the varied types of infection to which the method is applicable, but rather to consider the practical aspects of treatment involved.

If success is to be secured it will be necessary, in the consideration of any infection, to obtain certain definite information on the following points:

1. The localization of the infection, whether general or focal, whether pyemic or septicemic, whether saprophytic from retained necrotic tissue, whether acute or chronic, as well as other factors, such as local tension of the focus of infection under pressure, and the local blood-supply.

2. Definite knowledge of the predominating type of infection present and of the secondarily infecting organisms.

Speculation should not enter into the consideration of the rational worker, for, if definite knowledge in the application of the method is lacking — if hit-or-miss empirical therapy is employed — the guess may as well be wrong as right and the method discredited. One should remember that bacterial vaccines are toxic products, capable of good or harmful results, according to the method of use. No one will deny the value of morphin within certain limitations, but we all condemn its promiscuous administration. It is safe to conclude that if we depended more on first-hand information obtained by methods of clinical research and less on the advertisements of well-meaning manufacturers of biologic products, in which the evidences of clinical research are many times lacking, the practical results of bacterial therapy would be better.

The statement has repeatedly been noticed, in certain trade journals devoted to biologic products, that the use of vaccines can do no harm. One such journal† has recently recommended the use of mixtures of bacteria for such conditions as vertigo, pruritus ani, hay fever, rheumatism and sciatica. It has also published an article dealing with the treatment of gall-stones by vaccines and mentioned an abstract in which heart-block is spoken of as a streptococcus infection. The concern under whose auspices this journal is published has advertised at a recent medical meeting the use of vaccines in appendicitis. The motive in such instances is not difficult to discern. There may be some ground for the belief that if vertigo, as a symptom, is the result of middle-ear infection or infection of the sinuses, relief may be obtained through the administration of a suitable vaccine, providing free drainage is maintained. But it is, of course, irrational to advise the use of vaccines, without the preliminary bacteriologic knowledge first necessary, and to disregard other possible causes. Likewise in heart-block it is a far from desirable mental attitude to disregard the commonly known etiologic factors and to select a possible cause too remote for serious consideration.

RHEUMATISM

It may not be out of place at this time to speak of the therapy of rheumatism by a now well-advertised bacterial product called "Rheumatism Phylacogen." In the first place, the etiology of acute or chronic rheumatism is unknown and the treatment purely empirical. If the bacterial factors were known and could be isolated, it is possible that good results might be obtained from bacterial therapy. But until such knowledge is available, the treatment is speculative. To inoculate individuals with heterogeneous mixtures of bacteria, hoping to benefit those with gouty types of arthritis or those with atrophic eroded cartilages in arthritis deformans, both of which come under the broad conception of rheumatism, is of course ridiculous. It is not intended to convey the impression that joint manifestations and disability may not result from chronic focal infections elsewhere in the body. Instances are common due to chronic infected necrotic masses in the tonsils, to chronic sinusitis or to pyorrhea alveolaris, in which the joint manifestations clear up when the cause is removed. In such cases a supplemental course of vaccine therapy with the organisms isolated from the focus of infection, might augment the patients' resistance after the removal of the cause and as such would be rational treatment.

The preparation "Rheumatism Phylacogen," however, is made up of the metabolic products of a number of strains of pathogenic bacteria, and may truly be called a shotgun mixture with no scientific basis for its use. Other products such as "Gonorrhea Phylacogen," "Erysipelas Phylacogen" and "Mixed Infection Phylacogen" are on the market.

* An address before the Kent County Medical Society, Grand Rapids, Mich., Oct. 9, 1912.

† The Bacterial Therapist, G. H. Sherman, M.D., Editor.

In connection with this subject, it may be of interest to quote from a recent reply by the editor[1] of THE JOURNAL to a correspondent:

The resolution of our correspondent not to use this remedy since he knows nothing of it, except the information furnished by its promoters, is the proper one. Physicians have no moral right to employ remedies of whose nature they are ignorant, nor should they accept the statements of interested parties who fail to give them scientific information. "Rheumatism Phylacogen" is one of the series of proprietaries now being put on the market, based on a theory of the originator that it is possible and necessary in every infection, not only to combat the action of the principal causative agent, but also to counteract the influence of other organisms, supposed to be always present, which produce a mixed infection. For meeting this supposed mixed infection, a mixture of the metabolic products of a large number of organisms is made the base of the remedy to be administered. For instance, if the patient has pneumonia, the action of the pneumococcus may be aggravated by the streptococcus, and, therefore, a dose of streptococcus poison is added to the treatment. For fear the meningococcus may be overlooked, some of its metabolic products are added, and so forth. We have no definite information as to the particular organisms whose metabolic products enter into this "shotgun" base, so that the remedy is essentially a secret one. Moreover, as it is said to be produced by the action of pathogenic organisms, it must be of the nature of a toxin and presumably a dangerous one. In any event, until reliable, unbiased evidence as to its composition and action is available, it must be presumed that the injection of these toxins of unknown origin may have an injurious effect. . . .

The honest physician—one who is honest with himself and with his patients—will not lend himself to such experimentation. Let any one who undertakes the use of such a remedy remember that if bad results ensue, he, and not the manufacturer, will be held responsible.

I am aware that many physicians may be able to testify from their experiences that good results have been obtained from the use of these preparations. So are we familiar with many vaunted but now forgotten cures. The fact remains that such improvement as seemed to follow in certain instances has probably resulted in spite of the treatment, not because of it.

TUBERCLE INFECTIONS

In 1909 and 1910, I published the results we had been able to obtain in a limited number of cases of tuberculosis treated with different forms of tuberculin. In some of these opsonic determinations were made, in others the agglutination of the dead tubercle bacillus by the patient's serum, in others the precipitin reaction with the serum, while in others the clinical evidences alone served as a basis for the administration. None of these methods to control the administration of tuberculin sufficed in all cases; for what served as a sufficient immunizing response in one served to produce in others a prolonged negative phase of diminished resistance. I am convinced of the good results which may follow the administration of tuberculin in suitable cases, in suitable institutions, by men experienced in its use. As Pottenger has aptly said, "A hypodermic syringe filled with tuberculin cannot cure tuberculosis. It requires an intelligent brain to guide it."

There is at the present time, however, no adequate method of controlling the dosage. The opsonic index is but one of the methods of estimating the phase of immunity present, and since, in considering the index alone, we neglect other equally important phases of the process, such as the agglutinins, bacteriolysins and bactericidins, it is apparent that the knowledge obtained is incomplete. While half the truth is better than none at all, in this instance it does one little good, for it is a matter of common experience to see patients improve with a persistently low opsonic curve, while others may not be doing well with a persistently high index. I have never been able to satisfy myself that tuberculin-treated patients, in the aggregate, improved any more under its use than those without it.

I have, on the contrary, repeatedly seen harmful results from its indiscriminate use, in which, without careful attention to the clinical symptoms after each dosage, the physician blindly followed the serial dilution recommended by the manufacturer, with the result that he overwhelmed his patients with doses of toxins against which the immunizing machinery was already taxed to the utmost. There can be no doubt that lowered resistance, due to large doses of tubercle toxin, may be responsible for pleurisies with effusion developing in the course of otherwise favorably progressing lesions, for the suppuration occurring in glands which might otherwise have become healed with fibrous tissue, for hemoptysis which occasionally occurs, and for nephritis which may be transient or permanent.

There is much evidence to show that Nature makes the endeavor to auto-inoculate tuberculous individuals by setting free into the circulation toxins or endotoxins from the infected tissues through overactivity. If slight exercise causes a rise in temperature, with any marked degree of index alteration or with auscultatory changes over the lungs, it is certain that auto-inoculation is taking place. It is difficult and, indeed, practically impossible to control the degree of auto-inoculation by exercise, and patients who give evidence of continual auto-inoculation should have their amount of exercise restricted. This includes deep breathing.

The most favorable cases for vaccine treatment are those of chronic type in good nutrition and with no complications; those considered under the head of slowly advancing lung involvement with little or no fever, or other evidence of secondary infection, in whom, due either to an avirulent strain of bacillus or to good resisting powers, the progress of the disease is not rapid.

The acute early pulmonary cases with advancing involvement and active symptoms, such as rapid loss of weight and fever, will do better if the five classical essentials for the management of such cases are supplied, namely, (1) intelligent supervision, (2) fresh air, (3) sunshine, (4) good food and (5) rest.

In the treatment of tuberculous glands and sinuses, we are all aware of the unsettled controversy concerning the rôle played by bovine tubercle bacilli in these conditions. The consensus of opinion is against the view of Koch, who has reiterated his unbelief in the infectiousness of bovine tubercle for man. In intestinal tuberculosis, scrofulous glands and in many tuberculous sinuses leading from joints or bone, the bovine type of bacillus has been found. Dowd's[2] figures give 31 per cent. of twenty-nine cases of cervical tuberculous glands due to the bovine type. Moss[3] has stated that bovine bacilli were demonstrated in 20 per cent. of 306 tuberculous individuals, while the feeding experiments of Vansteenberghe and Grysez have proved that tubercle bacilli were absorbed by the intact intestinal mucosa and that extensive deposits were found later in the mesenteric glands, lungs and viscera. This may occur whether the human

1. Queries and Minor Notes, THE JOURNAL A. M. A., Aug. 10, 1912, p. 464.

2. Dowd, C. N.: Surg., Gynec. and Obst., March, 1909.
3. Moss, W. L.: Bull. Johns Hopkins Hosp., February, 1909.

or the bovine type is the infecting agent. Ritchie[4] has recorded undoubted cases of lung infection by bacilli of the bovine type and Grober's demonstration of a direct connection between the cervical lymphatics and the pleura and lungs explains the possibility of lung infection by either type of bacillus by extension from the tonsils.

Since then, in the consideration of this problem, without the elaborate laboratory facilities necessary to determine in each instance the type of organism present, whether in lung, pleura, gland or bone, it seems irrational to employ tuberculin promiscuously as a matter of experiment. It has certainly been natural to those of us who have watched the results obtained to question the advisability of its general use. On the other hand, if for one reason or another it is decided best to administer tuberculin, small doses, from 1/1,000 to 1/100 mg. according to Wright's method, have the advantage of comparative safety and are therefore to be recommended. In surgical tuberculosis, tuberculin therapy has given good results according to Hastings'[5] recent comprehensive article, if overdosage is carefully avoided and if attention is paid to the secondary infecting organisms. I doubt, however, if any surgeon can show that patients with tuberculous glands do not have so many recurrent operations under tuberculin treatment as those without it.

THE BACTERIEMIAS

I have had good results in the treatment, by means of an autogenous vaccine, of a few patients with streptococcus septicemia. On the other hand, I am not convinced, despite the rapid increase of favorable literature on the subject, that the results secured by vaccines will be any better than the results secured through the use, in suitable cases, of antistreptococcus or streptolytic serum and normal human serum. The results with bacterial vaccines have been gratifying in a few instances. In one patient, following an abortion between the third and fourth month of pregnancy, there was a rigor on the sixth day. The lochia were serosanguineous and foul in odor. Blood-cultures gave colonies of hemolytic streptococci on blood-agar. Some placental masses and clots were washed out of the uterus and an injection of 50 millions trivalent streptococcus stock vaccine was given. The temperature ranged from 103 to 104 F. The patient's condition was complicated by an infective periostitis and arthritis involving the right humerus and fibula. In all, six injections were given. The temperature reached normal on the seventh day of treatment, and the recovery of the patient was uneventful.

In this connection the work of Lea and Sidebotham[6] and of Heyemann[7] serves to bring to mind facts known before, but not generally appreciated, in reference to the presence of organisms in the parturient uterus. Lea and Sidebotham found that in 20 per cent. of fifty-eight cases hemolytic streptococci were present during the puerperium and yet produced no symptoms; while Heyemann found hemolytic streptococci in the lochia and blood of 17 per cent. of 125 puerperal cases with fever.

In Heyemann's series only those patients died whose blood contained streptococci, while those recovered in whose lochia, but not in whose blood, streptococci were found, even though accompanied by high temperature and evidence of serious infection.

The conclusion reached by these authors is that the presence of hemolytic streptococci in the lochia, or vaginal secretion, cannot, in itself, be considered an indication of systemic infection. It is obvious that in many cases of apparent septicemia the patients recover without specific therapy, and, as stated by Potter,[8] one must be careful in attributing the cure solely or partly to the treatment employed. The presence of hemolytic streptococci in the cavity of the parturient uterus undoubtedly increases the danger of systemic infection. It is a curious fact that such a comparatively large percentage of parturient uteri with fever contain them and no other serious symptoms follow.

In arriving at a diagnosis, by no cultural methods unfortunately can the virulent strains of organisms be differentiated from the non-virulent. It is essential, therefore, in order to obtain with certainty the strain doing the damage in septicemias, to obtain the culture for the preparation of the vaccine directly from the blood-stream. This is easily done by puncturing a vein with a sterile syringe with a capacity of from 2 to 5 c.c. containing a cubic centimeter or two of sodium citrate or ammonium oxalate solution to prevent clotting. The blood is then inoculated into tubes of sterile broth, ascitic broth or serum broth. If it is not possible to do this, a polyvalent vaccine corresponding to the predominant organisms present in the cavity of the uterus may be used. Probably from 70 to 80 per cent. of puerperal septicemias are due to streptococci or mixed infections of strepto-colon bacilli.

In considering the enormous mortality of puerperal septicemia, it goes without saying that vaccine inoculations or any method of rational procedure offering the slightest hope should be utilized. The attempt, so often made, however, to transfer active immunity in an animal by means of the blood-serum to a patient in this type of infection leads in a majority of cases to failure. On the other hand, I have seen beneficial results follow the use of antistreptococcus, streptolytic and normal human serum in a few cases of septicemia complicating tonsillitis and scarlatina. So far as I am aware there has been no reported recovery in *Streptococcus viridans* septicemia by any mode of treatment. These cases seem to be inevitably fatal.

Reasoning from present-day conceptions of the problems of immunity it may seem unreasonable to expect beneficial results to follow the administration of bacterial vaccines in the treatment of septicemic infections. In fact, the whole question is still *sub judice*. There can be no serious objection, however, to the use of appropriate serums as well as the use of bacterial vaccines in septicemia, when the dosage of the vaccines is controlled by appropriate bacteriologic studies so far as practicable in each case. In 1910, a patient with septic endocarditis and septicemia of six weeks' standing following curettage and septic thrombosis or embolism of pelvic veins was treated successfully by means of bacterial vaccines. The blood-culture showed a *Staphylococcus aureus*. The patient was given doses of from 200 to 300 millions every five days for about ten weeks; recovery followed, although of course the valvular damage was permanent.

Typhoid fever is a bacteriemia and as such has been treated by bacterial vaccines with beneficial results by

4. Ritchie, L. C. P.: Lancet, London, Nov. 16, 1907
5. Hastings, T. W.: Am. Jour. Med. Sc., August and September, 1912.
6. Lea, A. W. W., and Sidebotham, E. J.: Jour. Obst. and Gynec., Brit. Empire, January, 1909.
7. Heyemann, T.: Arch. f. Gynäk., 1908, lxxxvi, No. 1.
8. Potter, N. B.: Further Observations on Opsonins in Normal and Pathologic Serums, THE JOURNAL A. M. A., Nov. 30, 1907, p. 1815.

Watters and Eaton,[9] Callison,[10] Elliott,[11] Leishman,[12] and Meakins and Foster.[13] Bacterial therapy in typhoid is an open question, but, if used at all, the dosage should be large enough to secure evidence of protective response as measured by the only practical method now available, namely, increased agglutinative power on the part of the patient's blood. Smallman[14] has found that 300 millions represent the minimum efficient dose, although Watters and Eaton believe a dose of from 50 to 100 millions sufficient.

In typhoid fever, the varying virulence of different epidemics of the disease make it necessary to exercise care in the consideration of statistics as the result of any single form of treatment.

Typhoid vaccine may be used to advantage in the treatment of typhoid carriers. I have in the past two years reported two such instances.[15]

In gonococcic endocarditis and bacteriemia, I have seen beneficial results in one instance follow the use of antigonococcic serum and gonococcic vaccine. As mentioned above, there can be no serious objection to this method of treatment in any of the bacteriemias provided the necessary bacteriologic studies are made to insure appropriate correctness of diagnosis and dosage. In gonococcus arthritis, the sequel of bacteriemic invasion, good results may be expected from the use of bacterial vaccines, when combined, in my experience, with Bier's passive hyperemia. It has been found wise to begin with small doses, according to the virulence of the vaccine strain and to increase gradually, depending on signs of local and general reaction.

LOCALIZED STAPHYLOCOCCUS INFECTIONS

Possibly the most gratifying results in bacterial therapy have been obtained in the treatment of localized abscesses, furuncles or carbuncles due to staphylococci. I treat such conditions as follows: early incision to allow the escape of stagnant lymph, at which time a culture is taken; a Bier suction-cup is then applied for perhaps five minutes, after which a compress is applied, to be kept moist with a solution of sodium citrate 1 per cent. and sodium chlorid 2 per cent. This serves two purposes, to keep the flow of lymph by osmosis outward because the salt solution is hypertonic and to prevent the obstruction of free drainage, by clotting, since the lymph is decalcified by the sodium citrate. It is one of the essentials of bacterial therapy to keep at the point of infection a fresh supply of blood and tissue lymph. An injection of a stock staphylococcus vaccine is made until the autogenous vaccine is ready for use. The results by this mode of treatment have been better than by any other method. In fact, it may be stated that in any localized infection due to staphylococci, such as empyema wounds, sinuses, and adenitis, good results may be expected from bacterial vaccines providing free drainage and fresh blood-supply to the infected area are maintained.

In acne due to staphylococcus, the results have been good when combined with curettage of the face and hot applications to increase the blood-supply. With the acne bacillus vaccine our experience has not been satisfactory.

In one patient, the first to whom I applied the principle of vaccine therapy five years ago, an empyema pleurae following measles was treated by excision of a portion of two ribs and evacuation of nearly two quarts of pus. The lung gradually expanded and almost filled up the cavity, which, however, continued to discharge for five months. Antiseptic irrigations of all kinds were used and on several occasions the attempt was made to do away with the tube, but such attempts were followed by rise of temperature and chills. A culture from the wound showed *Staphylococcus aureus* from which a vaccine was prepared. After four inoculations, four to six days apart, the discharge was lessened. After six, the tube was removed permanently with prompt closure of the sinus. The patient has remained perfectly well.

In this connection, concerning the use of antiseptic irrigations in infected wounds, there is much to be said. Reasoning from our latter-day knowledge, little seems to be gained through their use except the mechanical removal of septic material, which can be as well accomplished by the use of a hypertonic salt solution, which tends to keep the flow of lymph by osmosis outward. We shall, in fact, accomplish much more by abstaining from the use of solutions damaging to the vitality of tissue, blood and lymph phagocytes thrown out in the wound area.

In six cases of staphylococcus sycosis a prompt cure followed two or three inoculations of a polyvalent staphylococcus vaccine. No other treatment was used except daily shaving and a bland ointment.

Ten cases of acute otitis media with perforation following influenza and measles were apparently benefited by the use of an autogenous vaccine. All were due to *Staphylococcus albus* and *aureus*. The discharge, which had been profuse for three or four weeks before the inoculations, was absent after two or three inoculations at five-day intervals. In two instances of chronic otitis media the *Bacillus pyocyaneus* was isolated. They were not improved by autogenous vaccines.

LOCALIZED GONOCOCCUS INFECTIONS

Any one who has treated a number of cases of gonorrheal vulvovaginitis in children realizes how difficult, prolonged and unsatisfactory the treatment is apt to be. The ordinary procedures — daily douches of mercuric chlorid or compound solution of cresol followed by swabbing the entire surface of mucous membrane with 25 per cent. argyrol or 1 to 2 per cent. silver nitrate solution, or, if the child is not too small, insufflations of protargol powder into the vagina after the method of Dr. Robert S. Walker, a method which should be more generally used — have been followed in my hands by bacteria-absent smears only after prolonged treatment. The use of a polyvalent vaccine, grown for some time on artificial mediums, has seemed materially to shorten the disease.

Vaccines prepared from freshly isolated strains of gonococci do not seem to give so good results as older strains and there appears to be no advantage gained from the use of an autogenous vaccine. The good results obtained by Butler and Long[16] and by Hamilton and Cook[17] are worthy of mention. Acute cases of gonorrheal

9. Watters, W. H., and Eaton, C. A.: Boston Med. and Surg. Jour., 1909, clx, 508; Med. Rec., 1909, lxxv, 93.
10. Callison, J. G.: Med. Rec., 1911, lxxix, 1129, 1161; Post-Graduate, 1911, xxvi, 718; Am. Jour. Med. Sc., 1912, cxliv, 350.
11. Elliott, J. B.: South. Med. Assn.; abstr. in THE JOURNAL A. M. A., Dec. 2, 1911, p. 1861.
12. Leishman, W. B.: Glasgow Med. Jour., 1912, lxxvii, 401; abstr. in THE JOURNAL A. M. A., July 27, 1912, p. 311.
13. Meakins, J. C., and Foster, L. S.: Canadian Med. Assn. Jour., 1911, i, 496.
14. Smallman: Jour. Royal Army Med. Corps, 1909, xii, 136.
15. Stone, W. J.: The Treatment of Typhoid Bacillus Carriers, THE JOURNAL A. M. A., Nov. 12, 1910, p. 1708; Am. Jour. Med. Sc., April, 1912.
16. Butler, W. J., and Long, J. P.: The Vaccine Treatment of Gonorrheal Vulvovaginitis in Children, THE JOURNAL A. M. A., March 7, 1908, p. 744.
17. Hamilton, A., and Cook, J. M.: Jour. Infect. Dis., 1908, ii, 178.

vulvovaginitis improve more rapidly as a rule under vaccine than those which receive the ordinary routine treatment. The best effects are to be expected in chronic cases. The opsonic index is not essential to treatment. I have treated several patients with gonorrheal inguinal adenitis by the injection of a polyvalent vaccine. One patient has been operated on twice for suppurating glands and part of them were removed each time. The remaining glands had subsequently become indurated and enlarged, and discharged a secretion, cultures from which showed a secondary infection with *Staphylococcus aureus*. A combination vaccine was used; the glands were much reduced in size after four injections and absent after six. In two other patients, the glands were enlarged to egg size, but were much reduced and the discharge absent after six to eight inoculations.

The dose of vaccine depends on the amount of the clinical reaction obtained. In gonorrheal arthritis this reaction consists of slight rise of temperature and malaise with increased tenderness and pain in the affected joints, lasting from six to twenty-four hours after an injection. The best results are apparently obtained when the dose is large enough to produce a slight reaction. I have rarely exceeded 25 millions with the strains making up my vaccine, but Cole and Meakins[18] have used from 300 millions to 1,200 millions in gonorrheal arthritis, while Irons[19] has used 20 millions to 500 millions.

LOCALIZED INFECTIONS WITH B. COLI COMMUNIS

I have treated about twenty infections following appendicitis due to the colon bacillus, in which the wound area was soiled, either at the time of operation through the rupture of an adherent fragile appendix or previously. Each of the patients was discharged with the wound healed on an average three and one-half weeks after operation. The purulent discharge was in each case profuse, but was lessened after the second or third inoculation with a vaccine prepared from the patient's organisms and begun as soon as possible after the pus appeared. The dose varied from 30 to 50 millions every third day. The average stay of twenty-five cases with wound infection treated in the same institution and under similar conditions, but without vaccine, was approximately six weeks as contrasted with three and one-half weeks for the twenty patients treated with vaccine.

The success of the treatment in one patient is worthy of mention. He had been operated on for appendical abscess eight weeks previously in a distant city. Following the operation there was a purulent discharge for six weeks; then the wound closed and the patient was allowed to leave the hospital. A few weeks afterward the wound opened. At this time pus and gas were discharged from the wound. A small perforation of the bowel at the bottom of the wound had taken place, and the patient was thoroughly septic. Pus also appeared in the urine, due to bladder infection from the abscess, and the bowel evacuations contained pus. A pure culture of the colon bacillus was obtained from the wound. An autogenous vaccine was made and an inoculation given every three to four days. After the second inoculation, the pus was diminished in the urine and from the wound. After three inoculations the wound was surgically clean; gas was no longer discharged and the wound soon healed. In all, four inoculations were given and the patient has remained well.

In cystitis due to the colon bacillus, so common in women, the results in many instances have been gratifying. One case cleared up after two inoculations. The patient had previously been treated by bladder irrigations and instillations, with little improvement during four weeks. In one patient with a fecal fistula following a lateral ileocolonic anastomosis, in which an autogenous colon vaccine was used, the results were not satisfactory. The leaking point in the bowel was so large as constantly to allow reinfection. In two cases of acute rectal fistula a colon vaccine was used with good results.

The result in one recent instance of pyelitis of pregnancy, due to the colon bacillus, is worthy of mention. At about the fifth month, this patient began to pass large quantities of pus and blood with the urine. The temperature ranged from 101 to 103 F. with occasional chills, which condition had persisted for about one month and was not amenable to any form of treatment by the attending physician. After the second dose of an autogenous vaccine, the temperature dropped by crisis to normal and so remained. In all ten or twelve doses were given. Varying quantities of pus persisted for several weeks thereafter, but the patient's general condition so much improved that she was delivered at term of a healthy child.

LOCALIZED PNEUMOCOCCUS INFECTIONS

In a self-limited acute disease like pneumonia, it does not appear that much can be accomplished by specific bacterial treatment. In "unresolved" pneumonia the use of a vaccine may be followed by good results. Patients with pneumonic empyema pleurae usually promptly recover with drainage, many of them by aspiration, but if complicated by secondary infection an appropriate vaccine will shorten the period of suppuration. In one patient with chronic frontal sinusitis and chronic empyema of the antrum, due to the *Micrococcus tetragenus* and the pneumococcus, in which an autogenous vaccine was used, the result was good after prolonged treatment.

In long-standing infections of this nature the lining of the cavities has become so altered through the formation of granulation tissue low in vitality, the so-called "pyogenic membrane," that it is difficult to bring to the area involved a sufficient amount of opsonin-containing blood. Likewise, in septic sinuses leading from a portion of necrotic bone, while the condition may be improved and the discharge of pus lessened through the use of a bacterial vaccine, little more than an amelioration of the symptoms may be expected until the necrotic bone is removed.

LOCALIZED STREPTOCOCCUS INFECTIONS

In tonsillitis and the adjacent adenitis, due to the streptococcus, good results may be expected from the use of a stock streptococcus vaccine. Likewise in infected sinuses leading from joints or bone, due to the streptococcus, good results may be expected providing free drainage and fresh blood-supply are secured. In the treatment of certain postscarlatinal complications, such as periostitis or localized abscesses due to streptococcus, the use of an autogenous vaccine is indicated. In erysipelas the results with stock streptococcus vaccine have been satisfactory when combined with local applications of a saturated solution of magnesium sulphate.

THE USE OF BACTERIAL PRODUCTS FOR DIAGNOSIS

An injection of gonococcic vaccine will often differentiate a gonorrheal joint from gout, rheumatic arthritis or tuberculosis. In a gonorrheal joint the pain, tenderness and redness are increased during the height of the

18. Cole, R. I., and Meakins, J. C.: Bull. Johns Hopkins Hosp., 1907, xviii, 223.
19. Irons, E. E.: Jour. Infect. Dis., 1908, iii, 279.

reaction, if the vaccine is potent and the dosage sufficient. On the other hand, excessive dosage is to be avoided, for what has been mentioned above in connection with tuberculin as detrimental to the interests of the patient and to the method, holds good in connection with any of the bacterial products. I have, on numerous occasions, seen an epididymitis follow so closely a large dose of gonococcus vaccine as to leave no doubt as to its cause.

In tuberculosis it is now generally conceded that the cutaneous reaction of von Pirquet, the reaction of Moro, the intradermal reaction of Mantoux and Moussu, the ophthalmic reaction of Calmette and the older method of subcutaneous injection have all been of value in diagnosis. My own preference in any doubtful condition has been for the subcutaneous injection of 1 mg. Old Tuberculin with the patient in bed, and to watch for subsequent auscultatory changes and fever. If no reaction occurs in two or three days, 5 mg. are injected and the focal symptoms watched as before. A third injection of 10 mg. may be given if necessary. One can assert, however, with considerable positiveness, if no focal or general symptoms follow the injection of 5 mg., that the patient has not an active tuberculosis.

A negative von Pirquet skin test is also of value in excluding a latent tuberculosis, although a positive reaction may not indicate that the process under consideration is then active. A positive reaction may only indicate that the individual has at some time had an active tuberculosis. It is true, on the other hand, that in active tuberculosis the reaction is often more intense than in the latent non-active types and as such is often of confirmatory value.

In typhoid fever, despite the statement of von Pirquet that a state of sensitization or allergy does not exist in this disease, Chantemesse[20] has described an ocular diagnostic test. He has used a dilution of the bacterial cellular proteids for instillation. The test has recently been applied by Austrian[21] in seventy-five cases of typhoid with positive results in seventy-one. As a diagnostic method the test gives much promise of usefulness.

Prendergast[22] has recently described a new test for typhoid which consists of the intradermal injection of a small dose, 5 millions, of typhoid vaccine. In the non-typhoid patient there becomes apparent within twenty-four hours an area of redness about the site of the injection, while in the patient with typhoid there is no reaction whatever. Such a test may have a negative if not a positive value.

THE USE OF BACTERIAL PRODUCTS FOR PROPHYLACTIC PURPOSES

To Wright must be given great credit for his pioneer work in the prophylaxis of typhoid fever by means of the injection of typhoid vaccine. The value of this work is just being appreciated. The results of such prophylaxis in the British, German and American armies are convincing. But the use of typhoid vaccine should be more general. In institutions where sporadic or endemic typhoid may arise, the well inhabitants should be immunized. This is particularly necessary in general hospitals where examples of contact infection among nurses, orderlies and physicians are common. In many large hospitals, all nurses, orderlies and interns are now immunized on beginning their service. Other progressive institutions should follow the example. It is to be hoped that as a means of furthering their sphere of usefulness, municipal boards of health will offer free immunization to all who apply. The cost will be small and the results will have great prophylactic and educational value. This will be especially worth while in localities where the disease is more or less constantly endemic. The immunity lasts from three to six years, possibly longer.

The recent studies of Sophian and Black[23] in prophylactic immunization against epidemic meningitis are worthy of special mention. They have been able to demonstrate increased agglutinins, from 1 in 200 to 1 in 1,500, in the patients' serum, after three injections of the vaccine; while immune bodies could be demonstrated by complement fixation as early as the fourth day after the first injection. The highest fixation was obtained in dilution 1 in 250 and occurred about three weeks after the beginning of vaccination. Three injections appeared to give the desired results; the first dose of 500 millions, the second and third of 1,000 millions each at weekly intervals. Some local and general reaction follows the injections but most of the symptoms have disappeared in from twenty-four to thirty hours. The immunity lasts at least one year.

Since epidemic meningitis is transmitted largely by healthy carriers of the meningococcus, vaccination of those who have been exposed and who themselves may be "contact carriers" becomes a matter of importance. The number of healthy carriers in an epidemic is much greater than the number who may be ill with the disease, but of course one can never be certain that a temporarily lowered resistance may not render the carrier susceptible. It would seem best, therefore, to vaccinate all exposed to the disease during an epidemic, especially those in whose families the disease has occurred as well as nurses, orderlies and physicians.

In scarlet fever we have attempted to immunize those exposed to the disease by means of a stock streptococcus vaccine. While we have had no instances of subsequent infection there are several factors which serve as argument against its use. The streptococcus has not been definitely shown to be the causative organism in the disease and if it were, the short period of incubation would probably leave insufficient time for immunization by vaccines.

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21. Austrian, C. R.: Bull. Johns Hopkins Hosp., 1912, xxiii, No. 251.
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23. Sophian, Abraham, and Black, J.: Prophylactic Vaccination Against Epidemic Meningitis, THE JOURNAL A. M. A., Aug. 17, 1912, p. 527.

PLEURAL EFFUSION DUE TO ARTIFICIAL PNEUMOTHORAX

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In a paper on the complications of artificial pneumothorax, Weiss[1] estimates that in about 50 per cent. of the cases an effusion develops on the treated side. In spite of this frequency there appear to be comparatively few American articles dealing with this subject, judging from the abstracted and complete papers which I have read.

Harris[2] records two cases, one occurring during the course of treatment, the other five months after discontinuing treatment. Pleurisy with effusion is reported

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2. Harris, S. T.: Treatment of Pulmonary Tuberculosis by Compression of Lung, Jour. Med. Assn. Ga., August, 1912; abstr., THE JOURNAL A. M. A., Aug. 24, 1912, p. 675.